

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	19	"707848"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/11 17:42
L2	12	"613687"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/11 17:55
L3	1786	de haan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	OFF	2006/05/11 17:56
L4	49	l3 and akzo	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	OFF	2006/05/11 18:07
L8	12	((("3340279") or ("4701450") or ("5037817") or ("4196188"))).PN	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/05/11 18:16

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S168	0	insulin secretion and (appetite suppressant)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/08 15:07
S169	60	insulin secretion and (appetite suppressant)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/08 15:07
S171	37	de haan pieter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:28
S172	9	S171 and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:34
S173	21	pieter and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:35
S175	2748	de haan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02
S176	0	"000513" and S175	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02
S177	0	"0005513" and S175	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02

EAST Search History

S17 8	12	S175 and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:10
S17 9	499	S175 and "2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:11
S18 0	2748	S175 and ay="2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:11
S18 1	216	S175 and @ay="2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:12
S18 3	1	"de haan" and @ay="2001" and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:12
S18 4	1	"6187339".PN.	USPAT; USOCR	NEAR	OFF	2006/05/09 16:14
S18 5	0	("6969708").URPN.	USPAT	NEAR	OFF	2006/05/09 16:16
S18 6	0	("2004/0229854").URPN.	USPAT	NEAR	OFF	2006/05/09 16:17
S18 7	0	("2004/0229854" "2006/0051420" "6399594" "6514958" "6969708").URPN.	USPAT	NEAR	OFF	2006/05/09 16:17
S19 0	1	"de haan" and @ay="2001" and menopau\$	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:19

EAST Search History

S19 2	43	haan pieter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/10 17:07
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Welcome to DIALOG

Dialog level 05.11.05D

Last logoff: 04may06 16:05:17

Logon file001 10may06 06:34:23

*** ANNOUNCEMENTS ***

NEW FILES RELEASED

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

DATABASES REMOVED

***File 196, FINDEX

***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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* * *

File 1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

Set Items Description

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Cost is in DialUnits

?

Terminal set to DLINK

? b 5,34, 155, 434

10may06 06:37:57 User291213 Session D12.1

\$0.40 0.114 DialUnits File1

\$0.40 Estimated cost File1

\$1.06 TELNET

\$1.46 Estimated cost this search

\$1.46 Estimated total session cost 0.114 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2006/May W1

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File 34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W5

(c) 2006 Inst for Sci Info

File 155:MEDLINE(R) 1951-2006/May 12
 (c) format only 2006 Dialog
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
 (c) 1998 Inst for Sci Info

Set	Items	Description
? s tiobolone		
S1	0	TIOBOLONE
? s tibolone		
S2	1659	TIBOLONE
? s s2 and release		
	1659	S2
	1038054	RELEASE
S3	20	S2 AND RELEASE
? rd		
S4	9	RD (unique items)
? s s4 and py<=2000		
Processing		
	9	S4
	44715778	PY<=2000
S5	3	S4 AND PY<=2000
? t s5/full/all		

5/9/1 (Item 1 from file: 5)
 DIALOG(R) File 5:Biosis Previews(R)
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0012765852 BIOSIS NO.: 200000484165
Gender differences and the effects of synthetic exogenous and non-synthetic estrogens in focal cerebral ischemia
 AUTHOR: Vergouwen Mervyn D I; Anderson Robert E (Reprint); Meyer Fredric B
 AUTHOR ADDRESS: Department of Neurosurgery, Mayo Clinic, 200 First Street
 SW, Rochester, MN, 55905, USA**USA
 JOURNAL: Brain Research 878 (1-2): p88-97 29 SEPTEMBER, 2000 2000
 MEDIUM: print
 ISSN: 0006-8993
 DOCUMENT TYPE: Article
 RECORD TYPE: Abstract
 LANGUAGE: English

ABSTRACT: The role of gender difference and estrogen in ischemic cerebrovascular events is controversial. Evidence is lacking as to whether or not there are significant gender differences in the incidence and outcome of stroke in the clinical setting. Recent clinical epidemiological studies have demonstrated that there is no significant association between the use of hormonal replacement therapy and the risk of stroke. However, several animal studies have shown that there are gender differences in stroke outcome and that exogenous administered estrogens are neuroprotective. In this study, the influence of gender differences and the effects of synthetic and non-synthetic estrogens were examined in a model of focal cerebral ischemia using 210 male, intact female, and ovariectomized female rats. All animals underwent 3 h of middle cerebral artery and bilateral common carotid artery occlusion. After 72 h, the rats were sacrificed and stained for histological assessment of infarction. There were no gender differences in infarction volume. Intravenous administration of either low or high dose 17beta-estradiol or tibolone did not alter infarct volume. Subcutaneous administration of low and high dose 17beta-estradiol using 7-day release pellets did not alter infarct volume. Low dose tibolone using implanted 7-day release pellets did not alter infarct volume. However,

high dose **tibolone** using implanted 7-day release pellets significantly ($P<0.05$) reduced infarct volume only in ovariectomized female rats. These results demonstrate that estrogen therapy has no effect on infarction volume following severe focal cerebral ischemia.

REGISTRY NUMBERS: 50-28-2: 17-beta-estradiol; 5630-53-5: **tibolone**

DESCRIPTORS:

MAJOR CONCEPTS: Nervous System--Neural Coordination; Pharmacology;

Cardiovascular System--Transport and Circulation

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: rat (Muridae)--animal model, female, male

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: focal cerebral ischemia--nervous system disease, vascular disease; stroke--nervous system disease, vascular disease, incidence, outcome

MESH TERMS: Brain Ischemia (MeSH); Cerebrovascular Disorders (MeSH)

CHEMICALS & BIOCHEMICALS: 17-beta-estradiol; synthetic exogenous estrogen; **tibolone**

METHODS & EQUIPMENT: hormone replacement therapy--therapeutic method

MISCELLANEOUS TERMS: sex difference

CONCEPT CODES:

20506 Nervous system - Pathology

10067 Biochemistry studies - Sterols and steroids

12512 Pathology - Therapy

14504 Cardiovascular system - Physiology and biochemistry

14508 Cardiovascular system - Blood vessel pathology

20504 Nervous system - Physiology and biochemistry

22002 Pharmacology - General

BIOSYSTEMATIC CODES:

86375 Muridae

5/9/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0011215837 BIOSIS NO.: 199800010084

Modulatory effects of a synthetic steroid (**tibolone**) and estradiol on spontaneous and GH-RH-induced GH secretion in postmenopausal women

AUTHOR: Genazzani Alessandro D (Reprint); Gamba Ombretta; Nappi Luigi; Volpe Annibale; Petraglia Felice

AUTHOR ADDRESS: Physiopathol. Human Reproduct., Univ. Modena, Via del Pozzo 71, 41 100 Modena, Italy**Italy

JOURNAL: Maturitas 28 (1): p27-33 Sept., 1997 1997

MEDIUM: print

ISSN: 0378-5122

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Objective: Since hormonal replacement therapy (HRT) affects plasma GH levels, the present study aimed to verify the effect of **tibolone** , a synthetic steroid, on modulating spontaneous and growth hormone releasing hormone (GH-RH) induced GH secretion. Methods: Postmenopausal women (n=30) were enrolled and randomly subdivided in three groups (n=10 each group): (1) treated with transdermal estradiol (50 mug) (Dermestrill, Rottapharm, Monza, Italy) biweekly; (2) treated with transdermal estradiol (100 mug) (Dermestrill. Rottapharm, Monza,

Italy) biweekly; (3) treated with **tibolone** 2.5 mg/day (Livial, Organon Italia, Rome, Italy). Patients underwent a GH-RH test (1 mug/kg) and 15 of them underwent to a pulsatility study before and 5 weeks after treatment. Results: Mean(+S.E.M.) GH plasma levels increased in all patients after any type of HRT. GH response to GH-RH stimulation (expressed as maximal response to GH-RH or as delta value) was similar in the three groups while significant changes occurred in spontaneous pulsatile GH release. **Tibolone** and both dosages of transdermal estradiol significantly reduced GH pulse frequency and increased pulse amplitude. Conclusions: The reduced plasma GH levels observed during postmenopause are probably related to a reduced endogenous GH-RH and not to a reduced pituitary ability to respond to GH-RH. In addition **tibolone**, as well as transdermal estradiol, are effective in restoring the spontaneous GH episodic release.

REGISTRY NUMBERS: 50-28-2: estradiol; 5630-53-5: **tibolone**

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--female, patient, postmenopausal

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CHEMICALS & BIOCHEMICALS: estradiol--estrogen-drug, hormone-drug, modulatory effects; **tibolone** --estrogen-drug, modulatory effects, synthetic steroid

METHODS & EQUIPMENT: hormonal replacement therapy--therapeutic method

MISCELLANEOUS TERMS: growth hormone-releasing hormone-induced growth hormone secretion; pulsatile growth hormone release

CONCEPT CODES:

22002 Pharmacology - General

10060 Biochemistry studies - General

16501 Reproductive system - General and methods

17002 Endocrine - General

BIOSYSTEMATIC CODES:

86215 Hominidae

5/9/3 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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03947633 Genuine Article#: QU412 Number of References: 67

Title: A COMPARATIVE-STUDY OF 2 HORMONE REPLACEMENT THERAPY REGIMENS ON SAFETY AND EFFICACY VARIABLES

Author(s): SISELES NO; HALPERIN H; BENENCIA HJ; BERG G; PILNIK S; MESCH V; ARRIGHI B; WIKINSKI RWW

Corporate Source: HOSP ITALIANO BUENOS AIRES,DIV GYNECOL,CLIMACTER SECT,ARAOZ 2241 PISO 3 C/BUENOS AIRES/DF/ARGENTINA/; HOSP FRANCES RIOSA/BUENOS AIRES/DF/ARGENTINA/; UNIV BUENOS AIRES,DEPT CLIN BIOCHEM/BUENOS AIRES/DF/ARGENTINA/

Journal: MATURITAS, 1995, V21, N3 (APR), P201-210

ISSN: 0378-5122

Language: ENGLISH Document Type: ARTICLE

Geographic Location: ARGENTINA

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine

Journal Subject Category: GERIATRICS & GERONTOLOGY; OBSTETRICS & GYNECOLOGY; MEDICINE, GENERAL & INTERNAL

Abstract: Objective: To assess the effect of **tibolone** on endometrial safety, plasma estradiol concentrations, lipid metabolism and climacteric symptoms in comparison to sequential conjugated equine estrogens and medroxyprogesterone acetate in postmenopausal women. Methods: In a randomised, open-label, 6-cycle, group-comparative study, the effects on the aforementioned parameters were studied with **tibolone** 2.5 mg/day (N= 13) continuously, and with conjugated equine estrogens 0.625 mg/day continuously, combined with medroxyprogesterone acetate 5 mg/day (N=11) (CEE/MPA) sequentially, during 12 days of each 28-day cycle. Within-group statistical analysis was performed with Student's t-test for paired samples, whereas between-group statistics were performed using the Student's t-test for independent groups. Results: Cytological evaluation revealed no endometrial stimulation in either group. In the **tibolone** group, there were no effects on estradiol levels, whereas in the CEE/MPA group, an increase in total and non-SHBG-bound estradiol plasma levels was reported. In the **tibolone** group, there were significant decreases in plasma total cholesterol, triglycerides, HDL-cholesterol and VLDL-cholesterol, whereas no significant changes in LDL-cholesterol and IDL-cholesterol were reported. In the CEE/MPA group there were significant decreases in plasma total cholesterol, HDL-cholesterol and LDL-cholesterol, whereas there were no significant changes in triglycerides, IDL-cholesterol and VLDL-cholesterol. Climacteric symptoms, particularly vasomotor episodes, decreased similarly in both groups. Conclusions: Both **tibolone** and CEE/MPA were safe with respect to effects on the endometrium and both treatments induced changes in the plasma profiles of certain lipid and lipoprotein parameters. However, the overall clinical implications of these changes are unknown. Finally, both regimens were equally effective in the treatment of climacteric symptoms.

Descriptors--Author Keywords: **TIBOLONE** ; **CONJUGATED EQUINE ESTROGENS** ; **MEDROXYPROGESTERONE ACETATE** ; **ESTROGEN** ; **LIPIDS** ; **CLIMACTERIC SYMPTOMS**
Identifiers--KeyWords Plus: **INTERMEDIATE-DENSITY LIPOPROTEINS** ; **CHOLESTEROL-FED RABBITS** ; **POSTMENOPAUSAL WOMEN** ; **ENDOMETRIAL CANCER** ; **POST-MENOPAUSAL** ; **AORTIC ACCUMULATION** ; **ESTROGEN THERAPY** ; **INCREASED RISK** ; **DOUBLE-BLIND** ; **ORG OD-14**

Research Fronts: 93-1862 001 (**HORMONE REPLACEMENT THERAPY** ; **POSTMENOPAUSAL WOMEN** ; **PERORAL ESTROGEN SUBSTITUTION**)

93-4872 001 (**TRANSDERMAL ESTROGEN REPLACEMENT THERAPY** ; **POSTMENOPAUSAL WOMEN** ; **SUSTAINED- RELEASE SUBDERMAL ESTRADIOL IMPLANTS**)

93-5772 001 (**ENDOMETRIAL CANCER IN POSTMENOPAUSAL WOMEN** ; **BODY-MASS INDEX** ; **PREVALENCE OF OBESITY** ; **RISK FOR CARDIOVASCULAR-DISEASE** ; **PROGNOSTIC FACTORS** ; **BRITISH ELDERLY**)

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BARENTSEN R, 1993, V51, P203, EUR J OBSTET GYN R B
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CUMMING DC, 1985, V61, P873, J CLIN ENDOCR METAB
CUST MP, 1990, V5, P345, DRUG SAFETY
DAWOOD MY, 1986, V155, P1246, AM J OBSTET GYNECOL
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 GENAZZANI AR, 1987, V1, P35, MATURITAS S1
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 HAARBO J, 1991, V87, P1274, J CLIN INVEST
 HAENGGI W, 1993, V31, P645, EUR J CLIN CHEM CLIN
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 HUNT K, 1990, V97, P1080, BRIT J OBSTET GYNAEC
 KABLE WT, 1990, V35, P512, J REPROD MED
 KICOVIC PM, 1982, V6, P81, REPRODUCCION
 KLOOSTERBOER HJ, 1990, V12, P37, MATURITAS
 KUPPERMAN HS, 1953, V6, P688, J CLIN ENDOCRINOL
 LAPOLLA JP, 1990, V163, P1055, AM J OBSTET GYNECOL
 LEFFLER H, 1963, V39, P313, AM J CLIN PATHOL
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 PARDRIDGE WM, 1986, V15, P259, CLIN ENDOCRINOL META
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 POWERS MS, 1985, V152, P1099, AM J OBSTET GYNECOL
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 RIJPKEMA AHM, 1990, V12, P259, MATURITAS
 RYMER J, 1993, V128, P259, ACTA ENDOCRINOL-COP
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 SHERWIN BB, 1989, V73, P759, OBSTET GYNECOL
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 STEINER G, 1987, V75, P124, CIRCULATION
 STUMPF PG, 1981, V52, P138, J CLIN ENDOCR METAB
 TAX L, 1987, V1, P3, MATURITAS S
 UTIAN WH, 1989, V161, P1828, AM J OBSTET GYNECOL
 VOLPE A, 1986, V8, P327, MATURITAS
 WEINSTEIN L, 1987, V69, P929, OBSTET GYNECOL
 WHITEHEAD M, 1988, V2, P1243, LANCET
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 WITTEMAN JCM, 1989, V298, P642, BRIT MED J
 ZIEL HK, 1975, V293, P1167, NEW ENGL J MED

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Set	Items	Description
S1	0	TIOBOLONE
S2	1659	TIBOLONE
S3	20	S2 AND RELEASE
S4	9	RD (unique items)
S5	3	S4 AND PY<=2000
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Welcome to DIALOG

Dialog level 05.11.05D

Last logoff: 04may06 16:05:17

Logon file001 10may06 06:34:23

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Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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File 1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

Set Items Description

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Cost is in DialUnits

?

Terminal set to DLINK

? b 5,34, 155, 434

10may06 06:37:57 User291213 Session D12.1

\$0.40 0.114 DialUnits File1

\$0.40 Estimated cost File1

\$1.06 TELNET

\$1.46 Estimated cost this search

\$1.46 Estimated total session cost 0.114 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2006/May W1

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File 34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W5

(c) 2006 Inst for Sci Info

File 155:MEDLINE(R) 1951-2006/May 12
 (c) format only 2006 Dialog
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
 (c) 1998 Inst for Sci Info

Set	Items	Description
? s tiobolone		
S1	0	TIOBOLONE
? s tibolone		
S2	1659	TIBOLONE
? s s2 and release		
	1659	S2
	1038054	RELEASE
S3	20	S2 AND RELEASE
? rd		
S4	9	RD (unique items)
? s s4 and py<=2000		
Processing		
	9	S4
	44715778	PY<=2000
S5	3	S4 AND PY<=2000
? t s5/full/all		

5/9/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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0012765852 BIOSIS NO.: 200000484165
Gender differences and the effects of synthetic exogenous and non-synthetic estrogens in focal cerebral ischemia
 AUTHOR: Vergouwen Mervyn D I; Anderson Robert E (Reprint); Meyer Fredric B
 AUTHOR ADDRESS: Department of Neurosurgery, Mayo Clinic, 200 First Street
 SW, Rochester, MN, 55905, USA**USA
 JOURNAL: Brain Research 878 (1-2): p88-97 29 SEPTEMBER, 2000 2000
 MEDIUM: print
 ISSN: 0006-8993
 DOCUMENT TYPE: Article
 RECORD TYPE: Abstract
 LANGUAGE: English

ABSTRACT: The role of gender difference and estrogen in ischemic cerebrovascular events is controversial. Evidence is lacking as to whether or not there are significant gender differences in the incidence and outcome of stroke in the clinical setting. Recent clinical epidemiological studies have demonstrated that there is no significant association between the use of hormonal replacement therapy and the risk of stroke. However, several animal studies have shown that there are gender differences in stroke outcome and that exogenous administered estrogens are neuroprotective. In this study, the influence of gender differences and the effects of synthetic and non-synthetic estrogens were examined in a model of focal cerebral ischemia using 210 male, intact female, and ovariectomized female rats. All animals underwent 3 h of middle cerebral artery and bilateral common carotid artery occlusion. After 72 h, the rats were sacrificed and stained for histological assessment of infarction. There were no gender differences in infarction volume. Intravenous administration of either low or high dose 17beta-estradiol or tibolone did not alter infarct volume. Subcutaneous administration of low and high dose 17beta-estradiol using 7-day release pellets did not alter infarct volume. Low dose tibolone using implanted 7-day release pellets did not alter infarct volume. However,

high dose **tibolone** using implanted 7-day release pellets significantly ($P < 0.05$) reduced infarct volume only in ovariectomized female rats. These results demonstrate that estrogen therapy has no effect on infarction volume following severe focal cerebral ischemia.

REGISTRY NUMBERS: 50-28-2: 17-beta-estradiol; 5630-53-5: **tibolone**

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MAJOR CONCEPTS: Nervous System--Neural Coordination; Pharmacology;

Cardiovascular System--Transport and Circulation

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: rat (Muridae)--animal model, female, male

COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: focal cerebral ischemia--nervous system disease, vascular disease; stroke--nervous system disease, vascular disease, incidence, outcome

MESH TERMS: Brain Ischemia (MeSH); Cerebrovascular Disorders (MeSH)

CHEMICALS & BIOCHEMICALS: 17-beta-estradiol; synthetic exogenous estrogen; **tibolone**

METHODS & EQUIPMENT: hormone replacement therapy--therapeutic method

MISCELLANEOUS TERMS: sex difference

CONCEPT CODES:

20506 Nervous system - Pathology

10067 Biochemistry studies - Sterols and steroids

12512 Pathology - Therapy

14504 Cardiovascular system - Physiology and biochemistry

14508 Cardiovascular system - Blood vessel pathology

20504 Nervous system - Physiology and biochemistry

22002 Pharmacology - General

BIOSYSTEMATIC CODES:

86375 Muridae

5/9/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0011215837 BIOSIS NO.: 199800010084

Modulatory effects of a synthetic steroid (tibolone) and estradiol on spontaneous and GH-RH-induced GH secretion in postmenopausal women

AUTHOR: Genazzani Alessandro D (Reprint); Gamba Ombretta; Nappi Luigi; Volpe Annibale; Petraglia Felice

AUTHOR ADDRESS: Physiopathol. Human Reproduct., Univ. Modena, Via del Pozzo 71, 41 100 Modena, Italy**Italy

JOURNAL: Maturitas 28 (1): p27-33 Sept., 1997 1997

MEDIUM: print

ISSN: 0378-5122

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Objective: Since hormonal replacement therapy (HRT) affects plasma GH levels, the present study aimed to verify the effect of **tibolone**, a synthetic steroid, on modulating spontaneous and growth hormone releasing hormone (GH-RH) induced GH secretion. Methods: Postmenopausal women (n=30) were enrolled and randomly subdivided in three groups (n=10 each group): (1) treated with transdermal estradiol (50 mug) (Dermestrill, Rottapharm, Monza, Italy) biweekly; (2) treated with transdermal estradiol (100 mug) (Dermestrill. Rottapharm, Monza,

Italy) biweekly; (3) treated with **tibolone** 2.5 mg/day (Livial, Organon Italia, Rome, Italy). Patients underwent a GH-RH test (1 mug/kg) and 15 of them underwent a pulsatility study before and 5 weeks after treatment. Results: Mean(+S.E.M.) GH plasma levels increased in all patients after any type of HRT. GH response to GH-RH stimulation (expressed as maximal response to GH-RH or as delta value) was similar in the three groups while significant changes occurred in spontaneous pulsatile GH release. **Tibolone** and both dosages of transdermal estradiol significantly reduced GH pulse frequency and increased pulse amplitude. Conclusions: The reduced plasma GH levels observed during postmenopause are probably related to a reduced endogenous GH-RH and not to a reduced pituitary ability to respond to GH-RH. In addition **tibolone**, as well as transdermal estradiol, are effective in restoring the spontaneous GH episodic release.

REGISTRY NUMBERS: 50-28-2: estradiol; 5630-53-5: **tibolone**

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: human (Hominidae)--female, patient, postmenopausal

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CHEMICALS & BIOCHEMICALS: estradiol--estrogen-drug, hormone-drug, modulatory effects; **tibolone** --estrogen-drug, modulatory effects, synthetic steroid

METHODS & EQUIPMENT: hormonal replacement therapy--therapeutic method

MISCELLANEOUS TERMS: growth hormone-releasing hormone-induced growth hormone secretion; pulsatile growth hormone release

CONCEPT CODES:

22002 Pharmacology - General

10060 Biochemistry studies - General

16501 Reproductive system - General and methods

17002 Endocrine - General

BIOSYSTEMATIC CODES:

86215 Hominidae

5/9/3 (Item 1 from file: 34)

DIALOG(R) File 34:SciSearch(R) Cited Ref Sci

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03947633 Genuine Article#: QU412 Number of References: 67

Title: A COMPARATIVE-STUDY OF 2 HORMONE REPLACEMENT THERAPY REGIMENS ON SAFETY AND EFFICACY VARIABLES

Author(s): SISELES NO; HALPERIN H; BENENCIA HJ; BERG G; PILNIK S; MESCH V; ARRIGHI B; WIKINSKI RWW

Corporate Source: HOSP ITALIANO BUENOS AIRES,DIV GYNECOL,CLIMACTER SECT,ARAOZ 2241 PISO 3 C/BUENOS AIRES/DF/ARGENTINA/; HOSP FRANCES RIOSA/BUENOS AIRES/DF/ARGENTINA/; UNIV BUENOS AIRES,DEPT CLIN BIOCHEM/BUENOS AIRES/DF/ARGENTINA/

Journal: MATURITAS, 1995, V21, N3 (APR), P201-210

ISSN: 0378-5122

Language: ENGLISH Document Type: ARTICLE

Geographic Location: ARGENTINA

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine

Journal Subject Category: GERIATRICS & GERONTOLOGY; OBSTETRICS & GYNECOLOGY; MEDICINE, GENERAL & INTERNAL

Abstract: Objective: To assess the effect of **tibolone** on endometrial safety, plasma estradiol concentrations, lipid metabolism and climacteric symptoms in comparison to sequential conjugated equine estrogens and medroxyprogesterone acetate in postmenopausal women. Methods: In a randomised, open-label, 6-cycle, group-comparative study, the effects on the aforementioned parameters were studied with **tibolone** 2.5 mg/day (N= 13) continuously, and with conjugated equine estrogens 0.625 mg/day continuously, combined with medroxyprogesterone acetate 5 mg/day (N=11) (CEE/MPA) sequentially, during 12 days of each 28-day cycle. Within-group statistical analysis was performed with Student's t-test for paired samples, whereas between-group statistics were performed using the Student's t-test for independent groups. Results: Cytological evaluation revealed no endometrial stimulation in either group. In the **tibolone** group, there were no effects on estradiol levels, whereas in the CEE/MPA group, an increase in total and non-SHBG-bound estradiol plasma levels was reported. In the **tibolone** group, there were significant decreases in plasma total cholesterol, triglycerides, HDL-cholesterol and VLDL-cholesterol, whereas no significant changes in LDL-cholesterol and IDL-cholesterol were reported. In the CEE/MPA group there were significant decreases in plasma total cholesterol, HDL-cholesterol and LDL-cholesterol, whereas there were no significant changes in triglycerides, IDL-cholesterol and VLDL-cholesterol. Climacteric symptoms, particularly vasomotor episodes, decreased similarly in both groups. Conclusions: Both **tibolone** and CEE/MPA were safe with respect to effects on the endometrium and both treatments induced changes in the plasma profiles of certain lipid and lipoprotein parameters. However, the overall clinical implications of these changes are unknown. Finally, both regimens were equally effective in the treatment of climacteric symptoms.

Descriptors--Author Keywords: **TIBOLONE** ; CONJUGATED EQUINE ESTROGENS ; MEDROXYPROGESTERONE ACETATE ; ESTROGEN ; LIPIDS ; CLIMACTERIC SYMPTOMS
Identifiers--KeyWords Plus: INTERMEDIATE-DENSITY LIPOPROTEINS; CHOLESTEROL-FED RABBITS; POSTMENOPAUSAL WOMEN; ENDOMETRIAL CANCER; POST-MENOPAUSAL; AORTIC ACCUMULATION; ESTROGEN THERAPY; INCREASED RISK; DOUBLE-BLIND; ORG OD-14

Research Fronts: 93-1862 001 (HORMONE REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; PERORAL ESTROGEN SUBSTITUTION)

93-4872 001 (TRANSDERMAL ESTROGEN REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; SUSTAINED- RELEASE SUBDERMAL ESTRADIOL IMPLANTS)

93-5772 001 (ENDOMETRIAL CANCER IN POSTMENOPAUSAL WOMEN; BODY-MASS INDEX; PREVALENCE OF OBESITY; RISK FOR CARDIOVASCULAR-DISEASE; PROGNOSTIC FACTORS; BRITISH ELDERLY)

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BARENTSEN R, 1993, V51, P203, EUR J OBSTET GYN R B
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 RIJPKEMA AHM, 1990, V12, P259, MATURITAS
 RYMER J, 1993, V128, P259, ACTA ENDOCRINOL-COP
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 STUMPF PG, 1981, V52, P138, J CLIN ENDOCR METAB
 TAX L, 1987, V1, P3, MATURITAS S
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 ZIEL HK, 1975, V293, P1167, NEW ENGL J MED

? ds

Set	Items	Description
S1	0	TIOBOLONE
S2	1659	TIBOLONE
S3	20	S2 AND RELEASE
S4	9	RD (unique items)
S5	3	S4 AND PY<=2000
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File 1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

Set	Items	Description
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Cost is in DialUnits		
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Terminal set to DLINK		
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10may06 06:42:24 User291213 Session D13.1		
	\$0.37	0.105 DialUnits File1
\$0.37	Estimated cost File1	
\$0.11	TELNET	
\$0.48	Estimated cost this search	
\$0.48	Estimated total session cost 0.105 DialUnits	

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2006/May W1
(c) 2006 BIOSIS
File 155:MEDLINE(R) 1951-2006/May 12
(c) format only 2006 Dialog

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? s particle()size		
	115385	PARTICLE
	843597	SIZE
S1	39949	PARTICLE()SIZE
? s drug()release		
	5058211	DRUG
	634193	RELEASE
S2	9496	DRUG()RELEASE
? s s1 and s2		
	39949	S1
	9496	S2
S3	1119	S1 AND S2
? s immediate()release or fast()release		
	168847	IMMEDIATE
	634193	RELEASE
	2163	IMMEDIATE(W)RELEASE
	198598	FAST
	634193	RELEASE
	552	FAST(W)RELEASE
S4	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
? s s1 and s2 and s3		
	39949	S1
	9496	S2
	1119	S3
S5	1119	S1 AND S2 AND S3
? s oral or peroral		
	737586	ORAL
	5841	PERORAL
S6	741667	ORAL OR PERORAL
? s oral or peroral or tablet?		
	737586	ORAL
	5841	PERORAL
	49590	TABLET?
S7	779168	ORAL OR PERORAL OR TABLET?
? s s1 and s2 and s4 and s7		
	39949	S1
	9496	S2

2714 S4
 779168 S7
 S8 8 S1 AND S2 AND S4 AND S7
 ? rd
 S9 6 RD (unique items)
 ? s s9 and py<=2001
 6 S9
 26962318 PY<=2001
 S10 3 S9 AND PY<=2001
 ? t s10/full/all

10/9/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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0012115461 BIOSIS NO.: 199900375121

Design and characterization of a surfactant-enriched tablet formulation for oral delivery of a poorly water-soluble immunosuppressive agent

AUTHOR: Ruddy Stephen B (Reprint); Matuszewska Bozena K; Grim Yvetta A; Ostovic Drazen; Storey David E

AUTHOR ADDRESS: Department of Pharmaceutical Research, Merck Research Laboratories, Merck and Co. Inc., WP78A-31, West Point, PA, 19486, USA**
 USA

JOURNAL: International Journal of Pharmaceutics (Amsterdam) 182 (2): p 173-186 May 25, 1999 1999

MEDIUM: print

ISSN: 0378-5173

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The feasibility of incorporating significant quantities of the anionic surfactant, sodium lauryl sulfate (SDS), into an **immediate release tablet** formulation of a poorly water-soluble immunosuppressive agent was investigated. Despite the extremely poor compressibility of SDS and poor chemical stability of the drug, a commercializable, direct-compression **tablet** formulation with satisfactory mechanical properties and acceptable chemical stability was achieved. Optimal in vitro release of the drug from the **tablet** formulation was achieved by establishing the minimum molar uptake ratio necessary to achieve complete micellar solubilization of the drug, after which formulation studies were conducted to determine the influence of formulation and process variables on the rate and extent of **drug release**. A model-independent analysis of dissolution results in a reduced volume (250 ml) of modified simulated gastric fluid demonstrated that the rate and extent of **drug release** was highly dependent on the mean **particle size** of the bulk drug, but independent of compression force above that required to achieve a compact of acceptable mechanical strength. Employing the Korsmeyer-Peppas model of Fickian and non-Fickian **drug release**, it was further shown that release of the drug from the dosage form was governed largely by surface erosion of the surfactant-enriched **tablet** matrix.

REGISTRY NUMBERS: 151-21-3: sodium lauryl sulfate

DESCRIPTORS:

MAJOR CONCEPTS: Chemistry; Pharmaceuticals--Pharmacology

CHEMICALS & BIOCHEMICALS: sodium lauryl sulfate--surfactant; L-733,725

--immunosuppressant-drug, in-vitro release, micellar solubilization,

surfactant-enriched **tablet** formulation, **oral** delivery, poorly

water-soluble

CONCEPT CODES:

22002 Pharmacology - General
10060 Biochemistry studies - General

10/9/2 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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12702315 PMID: 10794929

Application of Carbopol to controlled release preparations I. Carbopol as a novel coating material.

Muramatsu M; Kanada K; Nishida A; Ouchi K; Saito N; Yoshida M; Shimoaka A; Ozeki T; Yuasa H; Kanaya Y

Pharmaceutical Laboratories, Kissei Pharmaceutical Company, Limited, 4365-1 Kashiwabara, Hotaka, Minamiazumi, Nagano, Japan.

International journal of pharmaceutics (NETHERLANDS) Apr 10 2000 , 199 (1) p77-83, ISSN 0378-5173--Print Journal Code: 7804127

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We investigated the application of Carbopol(R) (CP) as a novel coating material prepared with various grades of CP having different degrees of cross-linking and molecular weights. Viscosity and spray mist size of CP aqueous solutions at various concentrations of CP were measured. Core **tablets** containing theophylline (TP), as a model drug, were coated with CP at various coating ratios. The TP release profile from the CP-coated **tablets** was studied by the JP13 paddle method. CP **tablets** were prepared by compressing CP powder, and the swelling behavior of the CP **tablets** in JP 1st fluid, purified water, and JP 2nd fluid was observed. The spray mist size of all CP aqueous solutions was small at a concentration of 1% and below, and drastically increased over a concentration of 1%. This result suggests that the appropriate concentration of the CP solution for coating is 1% or below. Sustained release of TP from the CP-coated **tablets** at a coating ratio of only 3% was observed in the JP 1st fluid and purified water, although **fast release** was observed in the JP 2nd fluid. The **fast release** in the latter fluid may be due to the fact that CP is an acid material. These results suggest that it is feasible to control the **drug release** by use of an extremely small amount of CP coating and that CP is useful as a novel coating material.

Descriptors: *Polyvinyls--chemistry--CH; Bronchodilator Agents--chemistry--CH; Cross-Linking Reagents; Drug Carriers; **Particle Size**; Solubility; **Tablets**, Enteric-Coated; Theophylline--chemistry--CH; Viscosity

CAS Registry No.: 0 (Bronchodilator Agents); 0 (Cross-Linking Reagents); 0 (Drug Carriers); 0 (Polyvinyls); 0 (Tablets, Enteric-Coated); 58-55-9 (Theophylline); 9007-20-9 (carboxypolymethylene)

Record Date Created: 20000725

Record Date Completed: 20000725

10/9/3 (Item 2 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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12253064 PMID: 10937289

Technology to obtain sustained release characteristics of drugs after delivered to the colon.

Hu Z; Kimura G; Ito Y; Mawatari S; Shimokawa T; Yoshikawa H; Yoshikawa Y; Takada K

Department of Pharmacokinetics, Kyoto Pharmaceutical University, Japan.

Journal of drug targeting (SWITZERLAND) 1999 , 6 (6) p439-48,

ISSN 1061-186X--Print Journal Code: 9312476

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

To determine the necessary technology by which sustained drug release is obtained after drug is delivered to the colon, two kinds of microcapsules were prepared and were filled in a pressure-controlled colon delivery capsule (PCDC). As a model drug 5-aminosalicylic acid (5-ASA) was used, because the target site of 5-ASA is the entire large intestine. 5-ASA was microencapsulated using a water-insoluble polymer, ethylcellulose (EC) or with pH-sensitive polymers, Eudragit L-100 or S-100 and encased in PCDC. The particle size of these microcapsules was around 800 microns and the loading efficiencies of 5-ASA were approximately 90%. In vitro dissolution tests were performed with the prepared microcapsules. The release rate of 5-ASA from the microcapsules was significantly prolonged as compared to 5-ASA powder, although there were no significant differences in the release rates between these microcapsules. By incorporating the 5-ASA microcapsules into PCDC, sustained release PCDCs for colon delivery were prepared and in vivo evaluation was performed using beagle dogs. As a fast release colon delivery system, PCDCs were prepared with 5-ASA powder suspended in suppository base. After oral administration of the test preparations to beagle dogs, plasma 5-ASA concentrations were measured and sustained release characteristics of 5-ASA from the test preparations were evaluated from the plasma 5-ASA concentration-time profiles. The first appearance time of 5-ASA into the systemic circulation after oral administration were 3 h for all the colon delivery preparations and it was thought that these test preparations were delivered to the colon. Both EC microcapsules and Eudragit S-100/RS-100 microcapsules in PCDC showed longer the mean residence time MRT, 8.2 +/- 0.6 h and 8.7 +/- 0.9 h, than Eudragit L-100/RS-100 microcapsules in PCDC where the MRT was 6.6 +/- 0.2 h. Since PCDCs containing 5-ASA powder exhibited a MRT of 7.0 +/- 1.0 h, these two types of preparations have suggested sustained release characteristics.

Tags: Male

Descriptors: *Colon--metabolism--ME; *Delayed-Action Preparations; Algorithms; Animals; Area Under Curve; Capsules; Cellulose--analogs and derivatives--AA; Chemistry, Physical; Dogs; Drug Delivery Systems; Excipients; Hydrogen-Ion Concentration; Injections, Intravenous; Mesalamine --blood--BL; Mesalamine--pharmacokinetics--PK; Polymethacrylic Acids; Powders; Solubility

CAS Registry No.: 0 (Capsules); 0 (Delayed-Action Preparations); 0 (Excipients); 0 (Polymethacrylic Acids); 0 (Powders); 25086-15-1 (methylmethacrylate-methacrylic acid copolymer); 89-57-6 (Mesalamine); 9004-34-6 (Cellulose); 9004-57-3 (ethyl cellulose)

Record Date Created: 20000829

Record Date Completed: 20000829

? ds

Set	Items	Description
S1	39949	PARTICLE() SIZE
S2	9496	DRUG() RELEASE
S3	1119	S1 AND S2
S4	2714	IMMEDIATE() RELEASE OR FAST() RELEASE
S5	1119	S1 AND S2 AND S3
S6	741667	ORAL OR PERORAL

S7	779168	ORAL OR PERORAL OR TABLET?
S8	8	S1 AND S2 AND S4 AND S7
S9	6	RD (unique items)
S10	3	S9 AND PY<=2001
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ds

Set	Items	Description
S1	39949	PARTICLE()SIZE
S2	57832	CRYSTALLINE
S3	266879	CRYSTAL?
S4	5134751	DRUG OR PHARMACEUTICAL
S5	741667	ORAL OR PERORAL
S6	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
S7	35	S6 AND S3
S8	27	S6 AND S3 AND S4
S9	20	RD (unique items)
S10	3	S6 AND S3 AND S4 AND S1
S11	2	RD (unique items)

? t s11/full/all

11/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0015240638 BIOSIS NO.: 200500147703

Observations in simultaneous microencapsulation of 5-fluorouracil and leucovorin for combined pH-dependent release

AUTHOR: Lamprecht Alf; Yamamoto Hiromitsu; Takeuchi Hirofumi; Kawashima Yoshiaki (Reprint)

AUTHOR ADDRESS: Lab Pharmaceut Engn, Gifu Pharmaceut Univ, 5-6-1 Mitahora Higashi, Gifu, 5028585, Japan**Japan

AUTHOR E-MAIL ADDRESS: yoshiaki@gifu-pu.ac.jp

JOURNAL: European Journal of Pharmaceutics and Biopharmaceutics 59 (2): p 367-371 February 2005 2005

MEDIUM: print

ISSN: 0939-6411 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: 5-Fluorouracil (5-FU) in combination with leucovorin (LV) is nowadays the standard treatment in colon cancer and would be a candidate to be delivered orally to the colon. Eudragit P-4135F or Eudragit RS100 were used separately to prepare microspheres by an oil/oil emulsification process trapping 5-FU and LV simultaneously. Scanning electron microscopy permitted a structural analysis, process parameters were analyzed and drug loading and release profiles were recorded. Particle size varied between 123 (RS100) and 146 Pm (P-4135F). Generally, higher encapsulation rates were found with RS100 (5-FU, 60.3 +/- 9.7%; LV, 81.4 +/- 8.6%) compared to P-4135F (5-FU, 48.3 +/- 2.0%; LV, 55.4 +/- 2.7%). Microparticles made from Eudragit RS100 released the incorporated drug combination within 8 h not exhibiting general differences between the kinetics of both drugs. P-4135F was found to maintain the undesired 5-FU release at pH 6.8 lower than 25% within 4 h. while at pH 7.4, a nearly immediate release (within 15 min) was observed. Although the release was similar at pH 7.4, at pH 6.8 LV showed a distinct initial drug loss of about 60% and a complete release within 2 h. SEM analyses revealed a substantial presence of LV crystals on the particle surface provoking a distinct burst effect of LV. These observations were concluded to be related to the high lipophilicity of P-4135F provoking a separation between P-4135F and LV during the preparation process. Copyright 2004 Elsevier B.V. All rights reserved.

REGISTRY NUMBERS: 51-21-8: 5-fluorouracil; 33434-24-1: Eudragit RS100;
58-05-9: leucovorin

DESCRIPTORS:

MAJOR CONCEPTS: Equipment Apparatus Devices and Instrumentation;
Gastroenterology--Human Medicine, Medical Sciences; Methods and
Techniques; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: colon--digestive system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates
DISEASES: colon cancer--digestive system disease, neoplastic disease,
drug therapy, prevention and control
MESH TERMS: Colonic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: 5-fluorouracil {5-FU}--antineoplastic- drug ,
drug regimen, oral administration, pharmacokinetics; Eudragit
P-4135F; Eudragit RS100; leucovorin {LV}--antineoplastic- drug , drug
regimen, oral administration, pharmacokinetics
METHODS & EQUIPMENT: Eudragit P-4135F microsphere-- drug delivery device
; Eudragit RS100 microsphere-- drug delivery device; scanning electron
microscopy {SEM} {scanning electron microscopy}--imaging and microscopy
techniques, laboratory techniques
MISCELLANEOUS TERMS: burst effect; combined pH-dependent drug release
; drug loading profile; drug release profile; encapsulation rate;
lipophilicity; particle size

CONCEPT CODES:

10060 Biochemistry studies - General
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
12512 Pathology - Therapy
14004 Digestive system - Physiology and biochemistry
14006 Digestive system - Pathology
22002 Pharmacology - General
22003 Pharmacology - Drug metabolism and metabolic stimulators
22005 Pharmacology - Clinical pharmacology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy

BIOSYSTEMATIC CODES:

86215 Hominidae

11/9/2 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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14234286 PMID: 12661666

Etanidazole-loaded microspheres fabricated by spray-drying different poly(lactide/glycolide) polymers: effects on microsphere properties.

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In this work, a spraying technique was used to encapsulate etanidazole (a
hypoxic radiosensitizer) into different poly(lactide/glycolide) polymers.

The properties of the obtained microspheres, especially the particle size and distribution, morphology and release rate were investigated. Unexpectedly, poly(L-lactide) (PLLA) shows a fast release rate, comparable to PLGA 50: 50, due to the dissociation of the microspheres although the release rate of the spray-dried microspheres of other polymers decreases with increasing lactide ratio. It is also interesting to note that, contrary to the viscosity sequence of the polymer solutions, the particle size of the microspheres decreases in the order PLGA 50: 50, PLGA 65: 35, PLGA 85: 15 and PDLA. The morphology of microspheres can be affected by polymer properties (e.g. lactide/glycolide ratio, molecular weight, crystallinity and Tg) and fabrication conditions (e.g. solvent and polymer concentration to be sprayed). Although most of the microspheres fabricated by EA have a doughnut-like shape with smooth surface, it is possible to obtain spherical particles by choosing proper polymer type and polymer concentration. A further examination of the mechanisms of the atomization process and the solvent evaporation process reveals their respective effect on droplet formation and particle formation, both of which are essential for the spray-drying technique. It is found that polymer phase transition (affected by the polymer solubility) and its subsequent solvent evaporation processes can finally determine the morphology and the particle size of the spray-dried particles made from different polymers. In essence, the lactide/glycolide ratio of the polymers plays a more important role in affecting the properties of the spray-dried microspheres.

Descriptors: *Biocompatible Materials; *Etanidazole; *Microspheres; *Polyglactin 910; Calorimetry, Differential Scanning; Delayed-Action Preparations; Drug Carriers; Microscopy, Electron, Scanning; Polyglactin 910--chemistry--CH; Radiation-Sensitizing Agents; Research Support, Non-U.S. Gov't; Viscosity

CAS Registry No.: 0 (Biocompatible Materials); 0 (Delayed-Action Preparations); 0 (Drug Carriers); 0 (Radiation-Sensitizing Agents); 22668-01-5 (Etanidazole); 34346-01-5 (Polyglactin 910)

Record Date Created: 20030328

Record Date Completed: 20031120

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Set	Items	Description
S1	39949	PARTICLE()SIZE
S2	57832	CRYSTALLINE
S3	266879	CRYSTAL?
S4	5134751	DRUG OR PHARMACEUTICAL
S5	741667	ORAL OR PERORAL
S6	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
S7	35	S6 AND S3
S8	27	S6 AND S3 AND S4
S9	20	RD (unique items)
S10	3	S6 AND S3 AND S4 AND S1
S11	2	RD (unique items)